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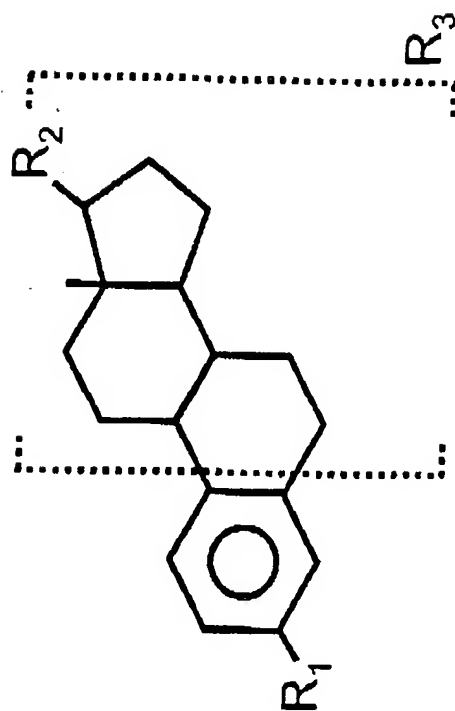


Figure 1: General structure of activators of non-genomic Estrogen-Like Signalling (ANGELS).

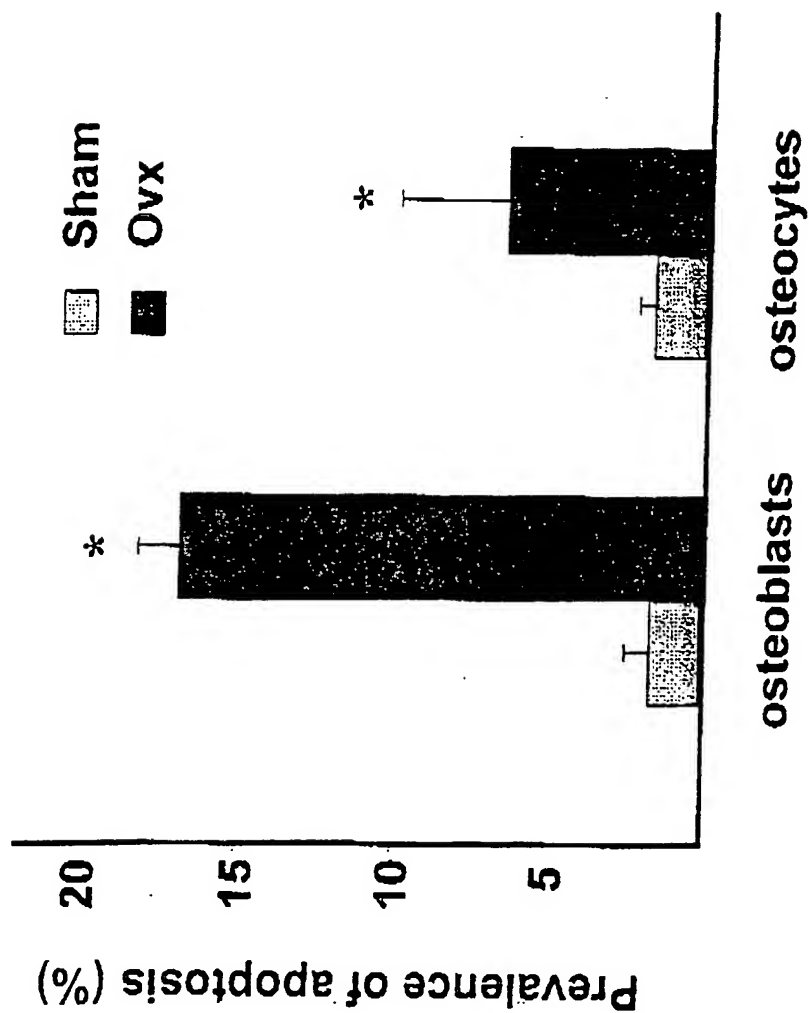


Figure 2: Estrogen deficiency causes increased apoptosis of osteoblasts and osteocytes in murine vertebral bone.

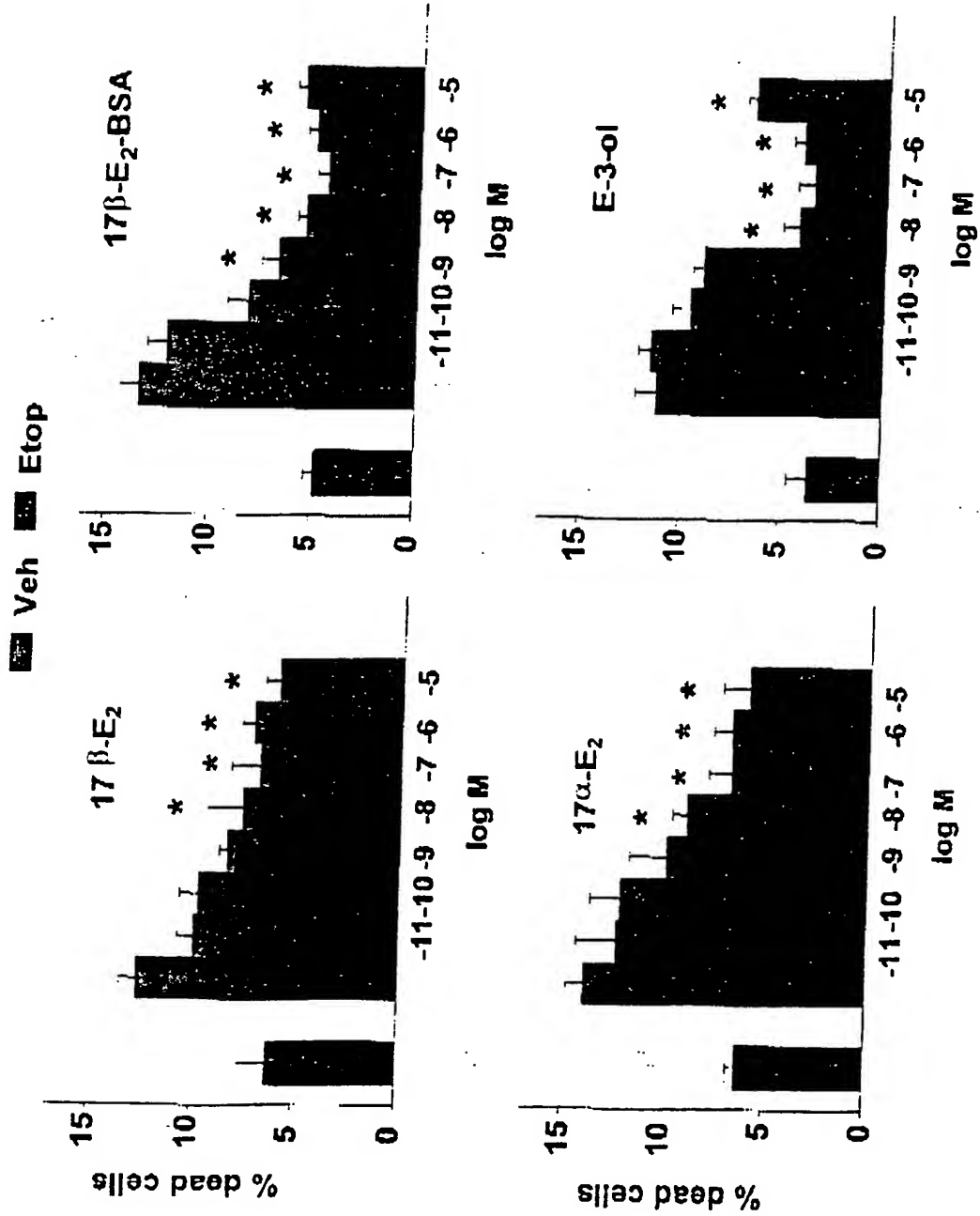


Figure 3: Inhibition of apoptosis of osteoblastic cells.

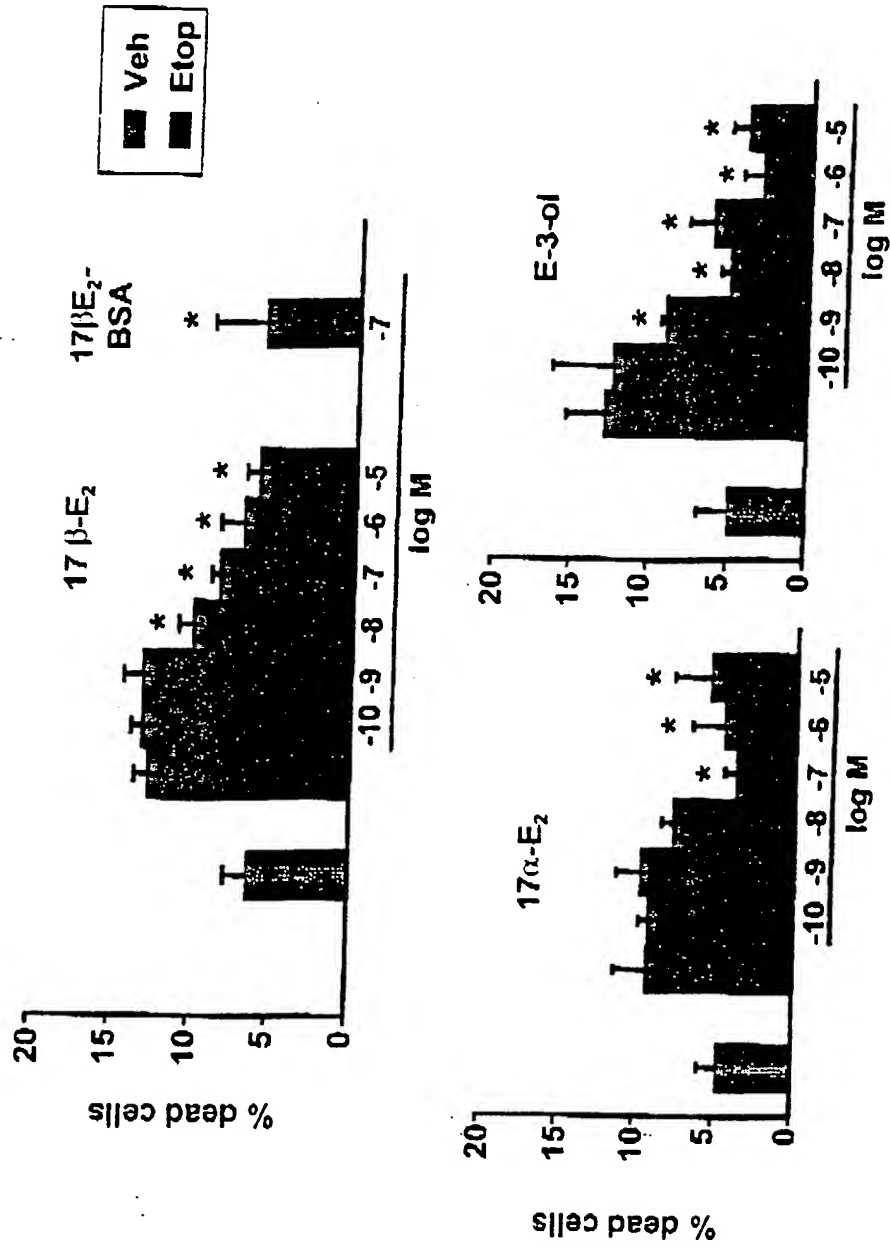


Figure 4: Inhibition of apoptosis of MLO-Y4 osteocytic cells by ANGELS

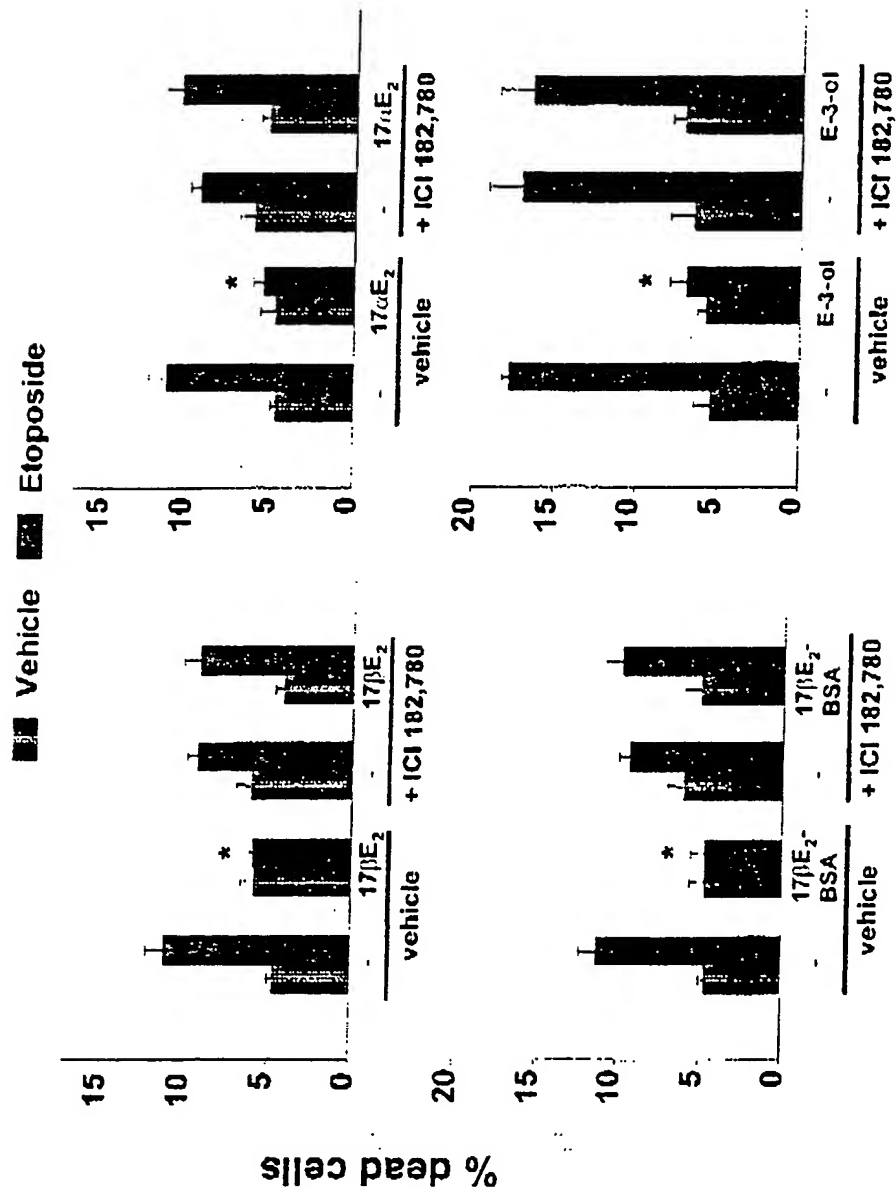


Figure 5: Blockade of the anti-apoptotic effect of estrogen and ANGELS by ICI 182,780 in osteoblastic cells

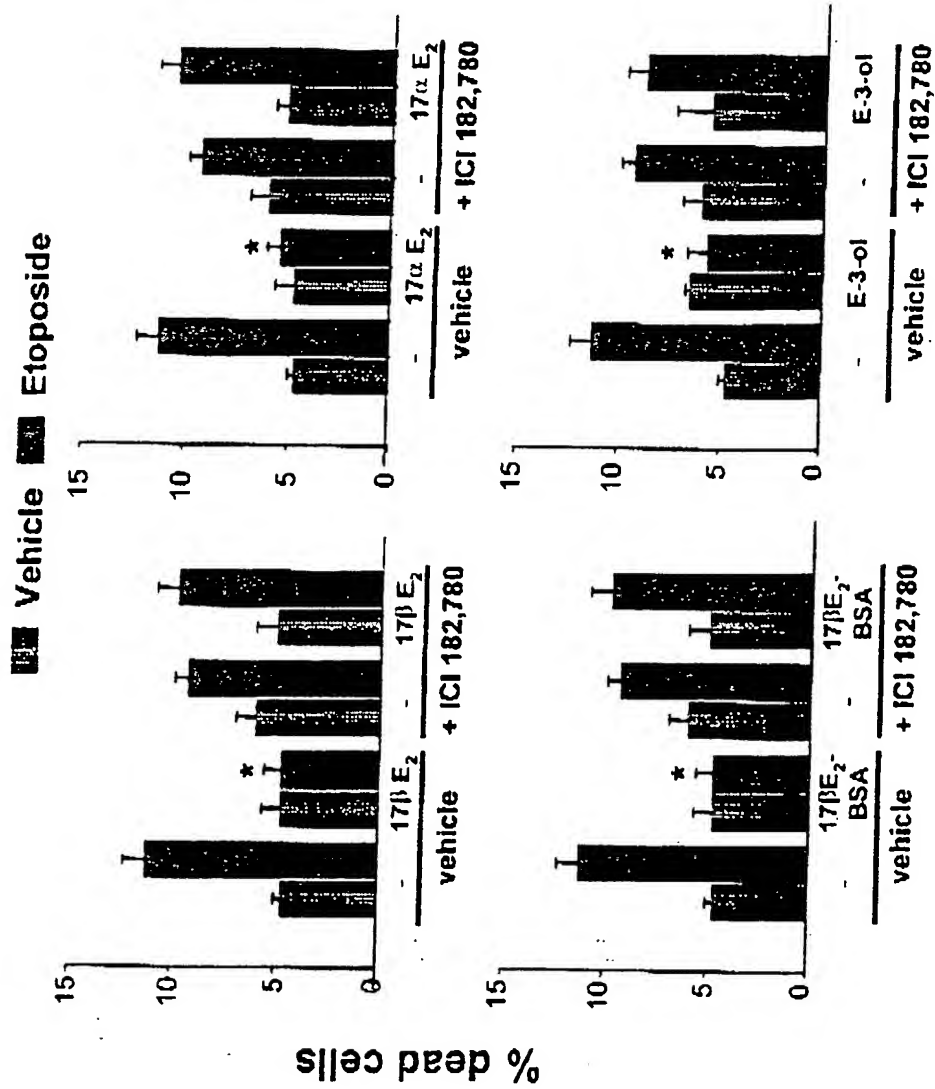


Figure 6: Inhibition of the antiapoptotic effect of estrogen and ANGELS by ICI 182,780 in MLO-Y4 osteocytic cells

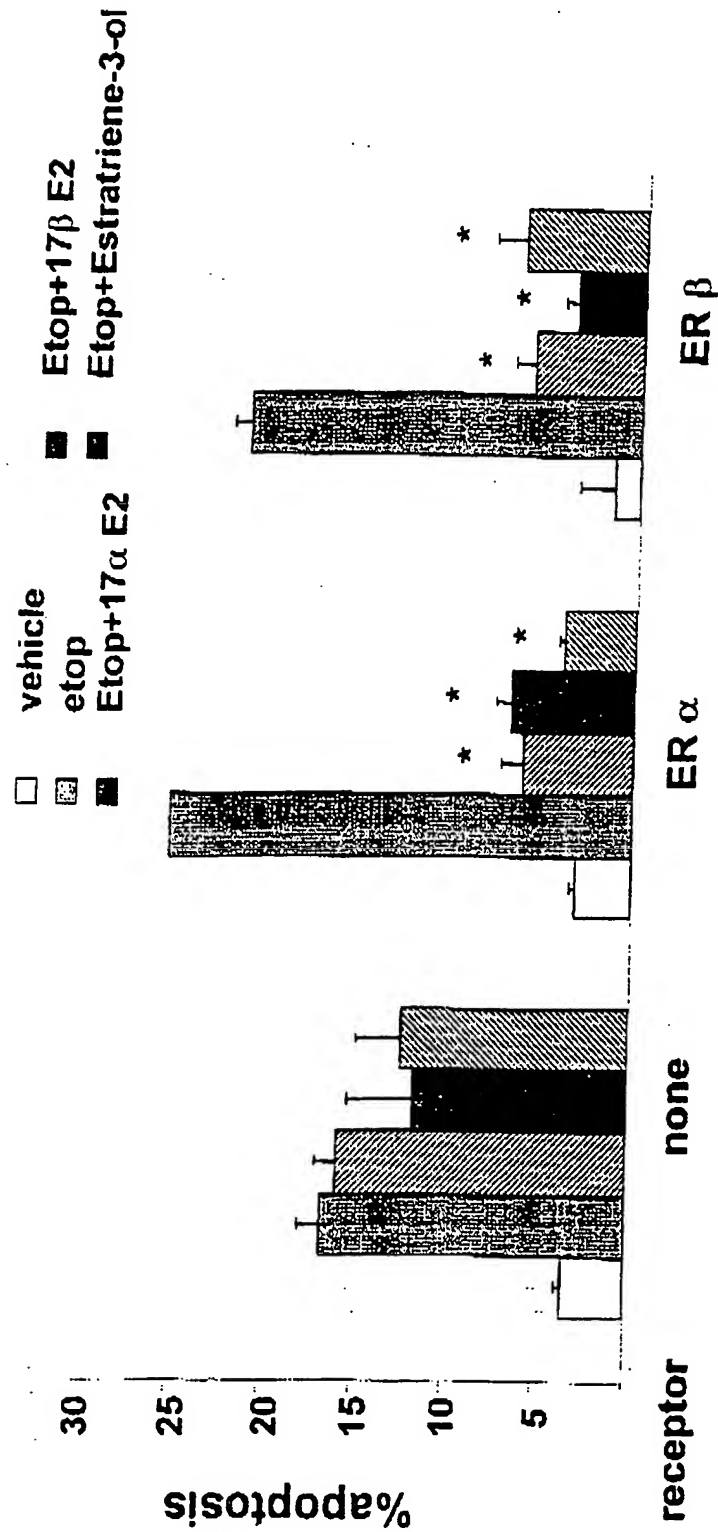


Figure 7: Estrogen receptor α or β is required for the antiapoptotic effects of 17 β estradiol, 17 α estradiol, and estratriene-3-ol on etoposide-induced apoptosis (experiment 1/21/99).

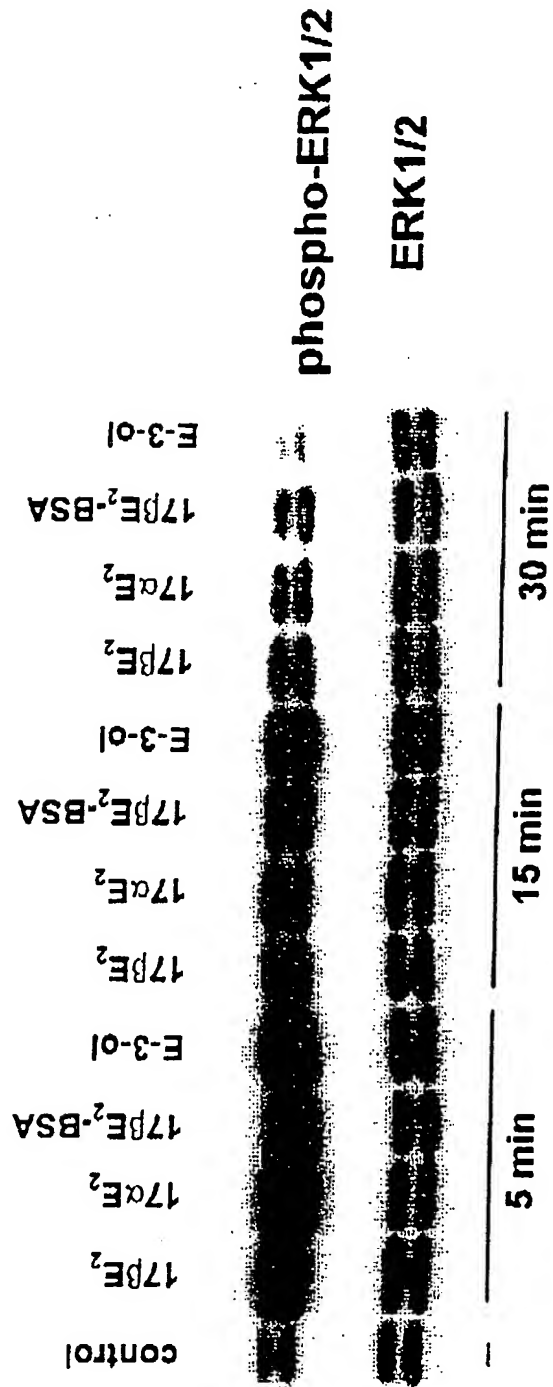


Figure 8: Activation of Extracellular Signal Regulated Kinases (ERKs)

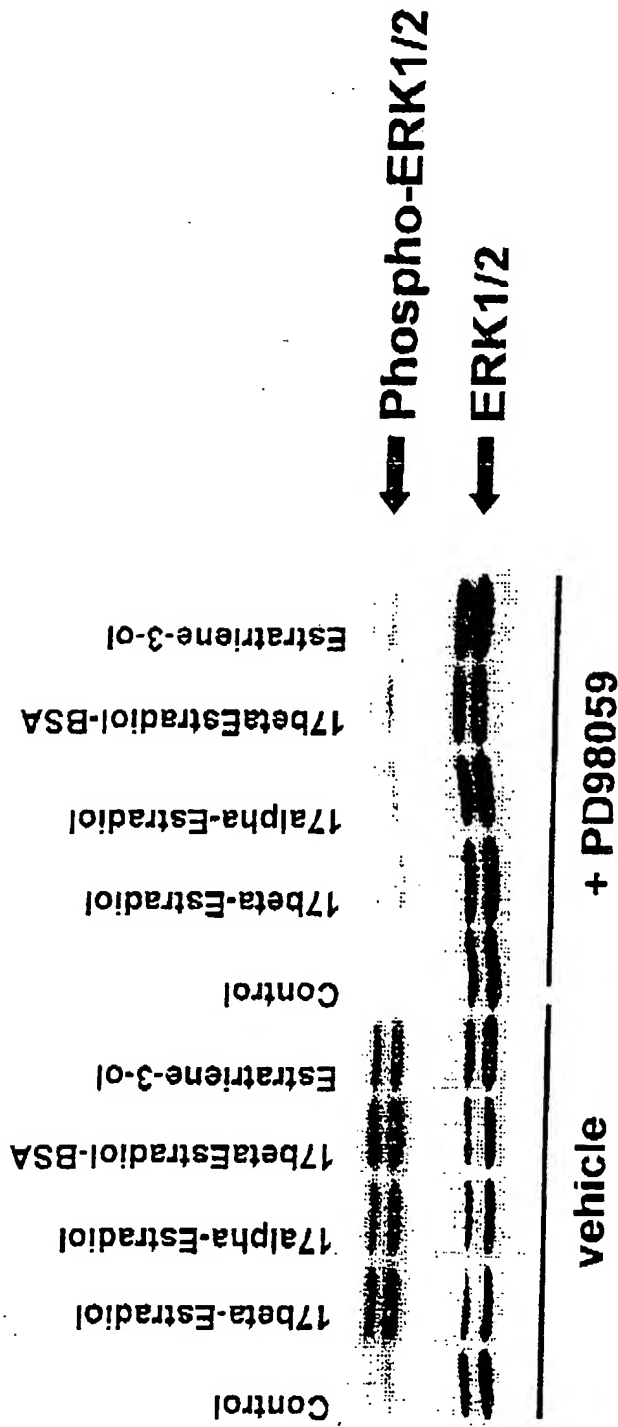


Figure 9: The effect of estrogenic compounds on the activation of ERK1/2 is blocked by a specific inhibitor.

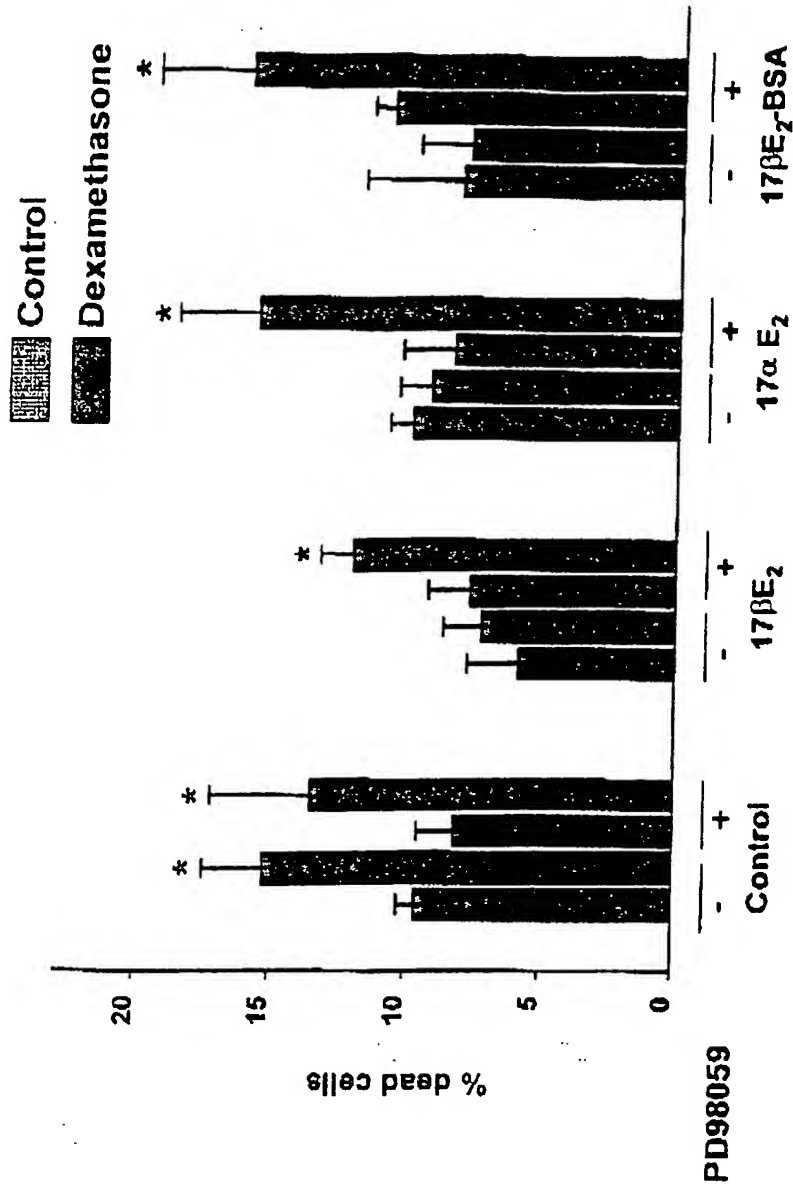


Figure 10: The specific inhibitor of ERK activation abolishes the anti-apoptotic effect of the estrogenic compounds.

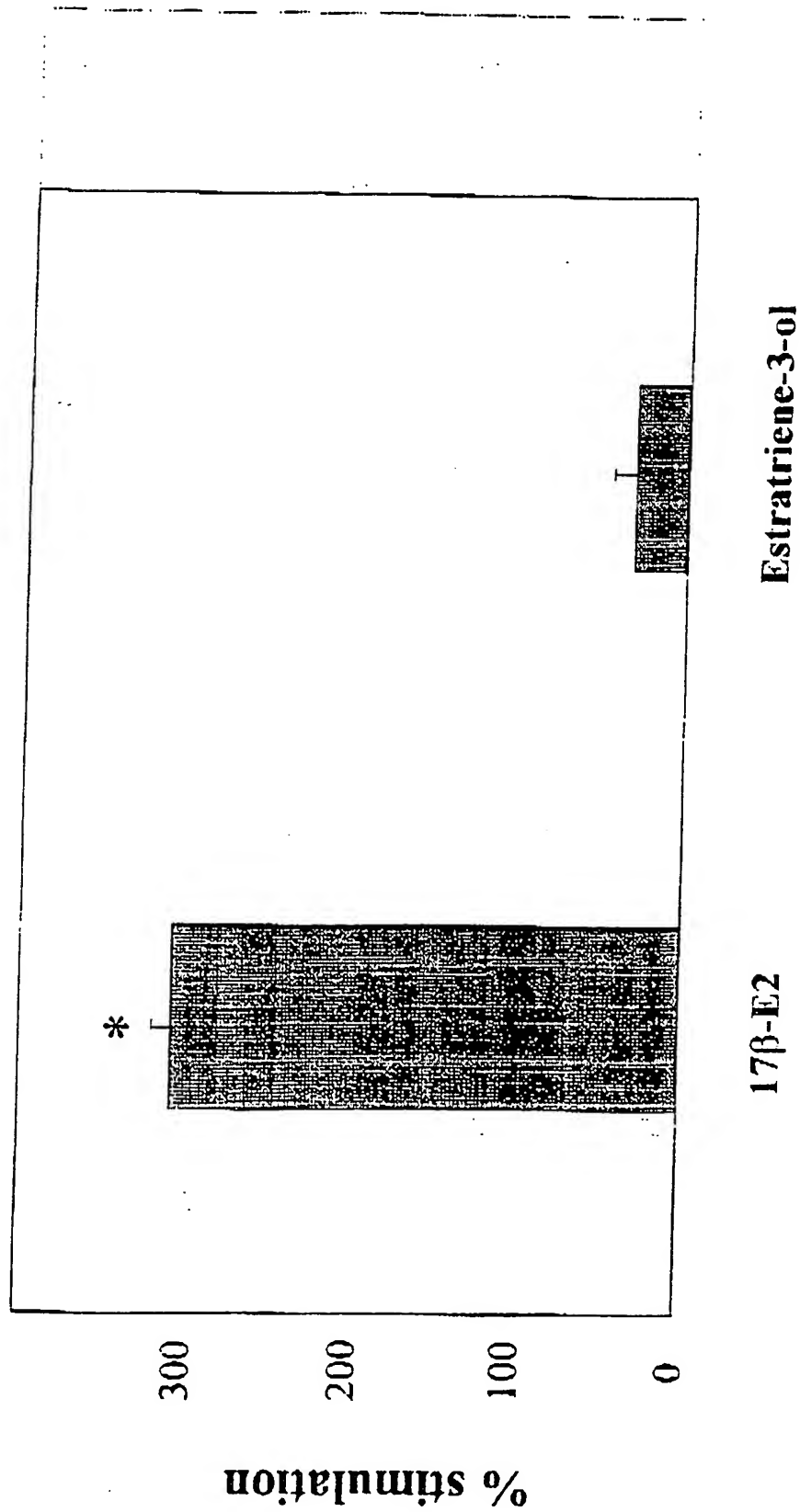
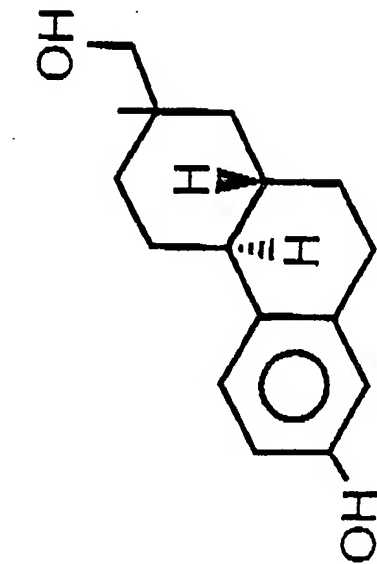
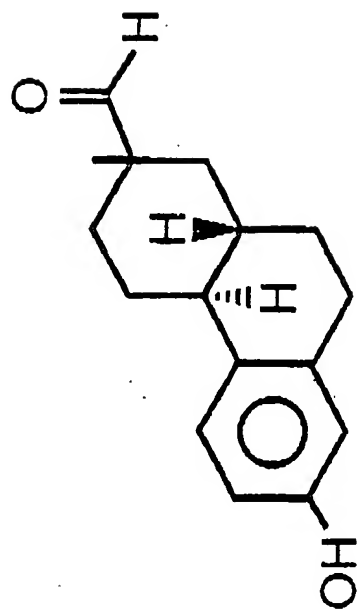


Figure 11 : Unlike 17β estradiol, estradiene-3-ol does not transactivate an estrogen response element through ER α .



$C_{16}H_{22}O_2$
MW=246

[2S-(2a,4a α ,10a β)]-1,2,3,4,4a,9,10,10a-Octahydro-7-hydroxy-2-methyl-2-phenanthrenemethanol



$C_{16}H_{20}O_2$
MW=244

[2S-(2a,4a α ,10a β)]-1,2,3,4,4a,9,10,10a-Octahydro-7-hydroxy-2-methyl-2-phenanthrenecarboxaldehyde

Figure 12

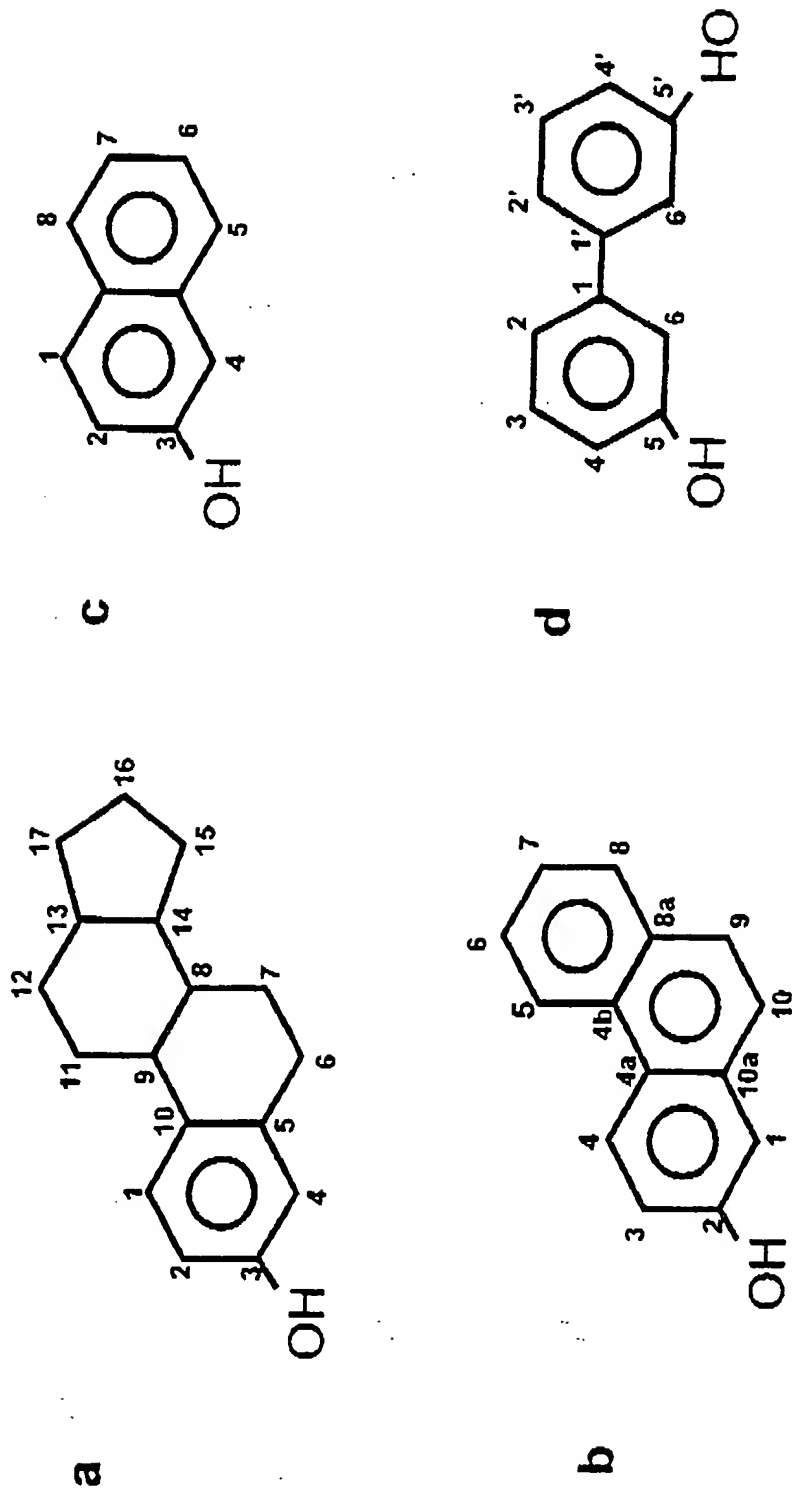


Figure 13

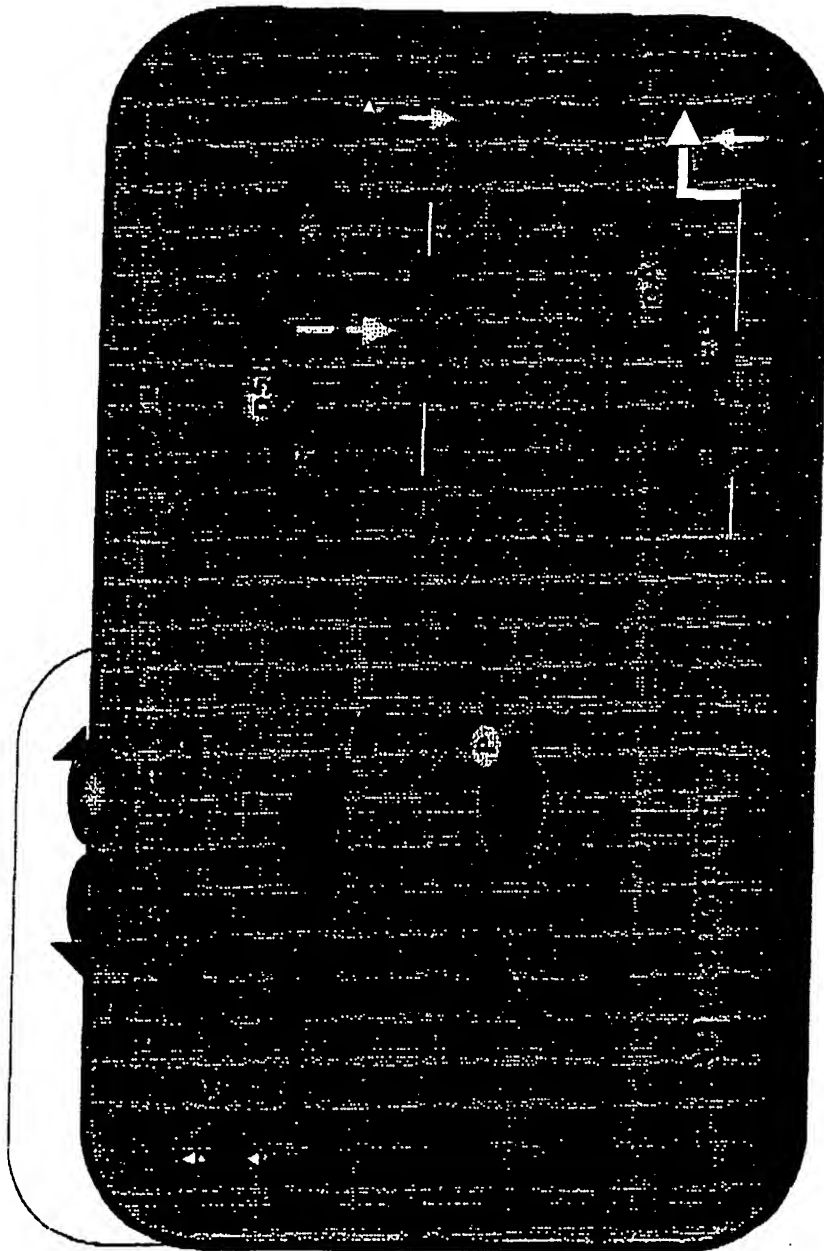


Figure 14: Mechanisms of Estrogen Receptor Action

Formation occurs only on sites of previous osteoclastic bone resorption.

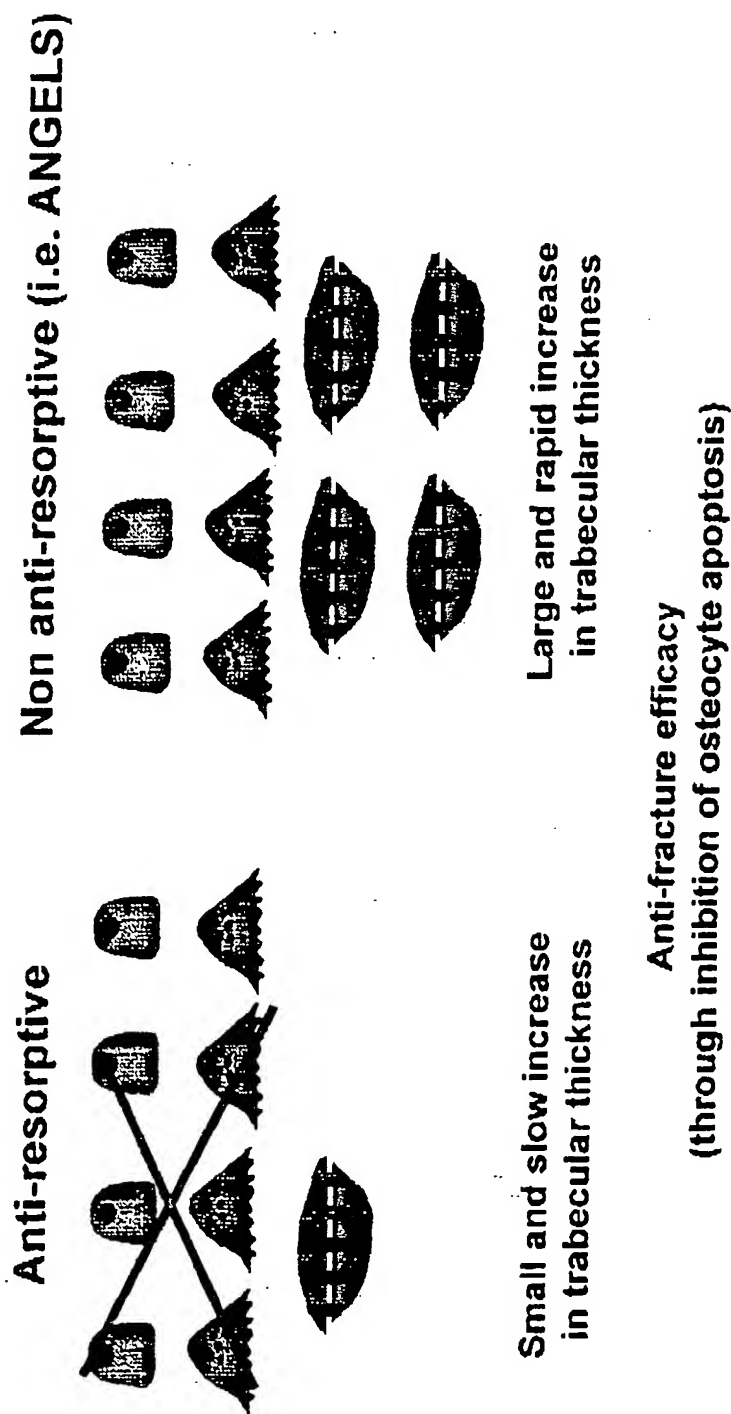


Figure 15: Implications of the effects of anti-resorptive vs. non anti-resorptive agents on apoptosis

R AND/OR R' SUBSTITUTION	
	STRUCTURE
HYDROXY-	$-OH$
METHYL-	$-CH_3$
METHOXY-	$-OCH_3$
ACETOXY-	$O-\underset{\text{C}}{\overset{\text{O}}{\text{C}}}-CH_3$
ETHOXY-	$O-CH_2-CH_3$
3,3-DIMETHOXY-	$\begin{array}{c} \diagup OCH_3 \\ \diagdown OCH_3 \end{array}$
ETHYNYL-	$\begin{array}{c} \diagup C \equiv CH \\ \diagdown O \end{array}$
BENZOYLOXY-	$O-\underset{\text{C}}{\overset{\text{O}}{\text{C}}}-\text{C}_6\text{H}_5$
BENZYL OXY-	$OCH_2-\text{C}_6\text{H}_5$
GLUCURONYL-	$C_6H_8O_5$
SULFATE SODIUM-	OSO_3Na
CARBOXY-	$=O$
VALERYLOXY-	$-C_5H_9O$
CYCLOPENTYLPROPYLOXY-	$-O-\underset{\text{C}}{\overset{\text{C}}{\text{C}}}-(CH_2)_2-\text{C}_5\text{H}_9$
PROPYLOXY-	$-O-\underset{\text{C}}{\overset{\text{C}}{\text{C}}}-CH_2-CH_2-CH_3$
HEMISUCCINYL-	$-C_4H_4O_3$
PALMITOXY-	$-C_{16}H_{32}O_2$

Figure 16A

R ₁ AND/OR R ₂ SUBSTITUTIONS	STRUCTURE
SODIUM PHOSPHATE	$-O-PO_3Na_2$
ENANTHATE	$-C_7H_{12}O$
GLUCURONIDE SODIUM SALT	$-C_6H_8O_6Na$
STEARATE	$-C_{18}H_{34}O$
TRIETHYL AMMONIUM SALT	$-N-(C_2H_5)_3$
CYCLOPENTYL	$O-\overset{\overset{O}{\parallel}}{C}-CH_2CH_2-\text{Cyclopentyl}$

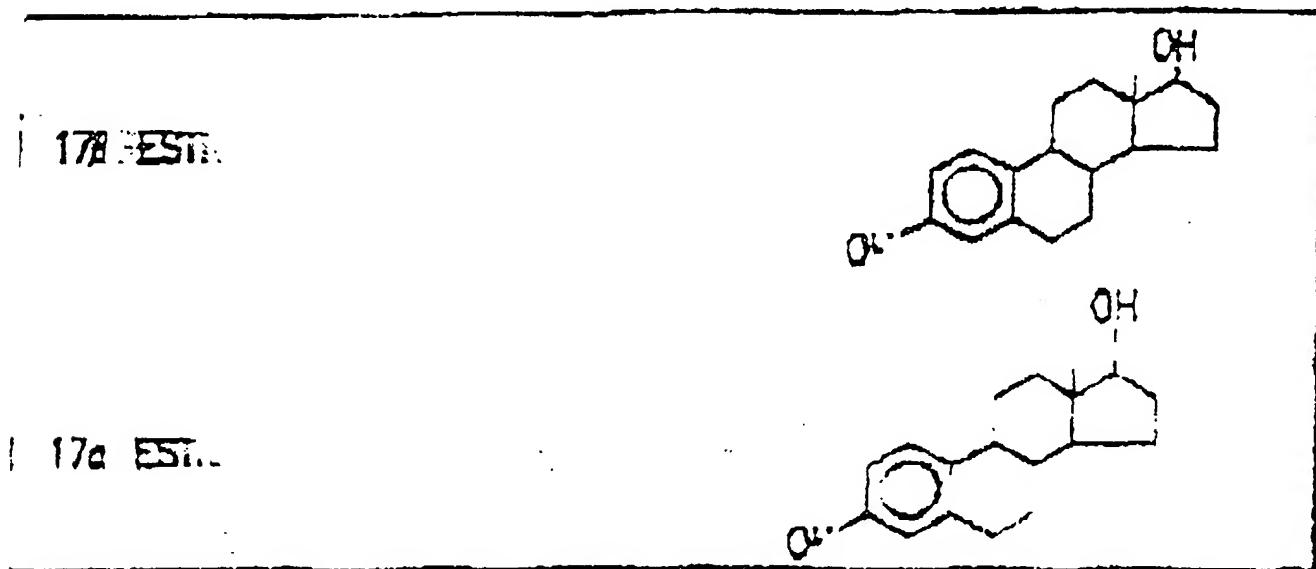


Figure 16B

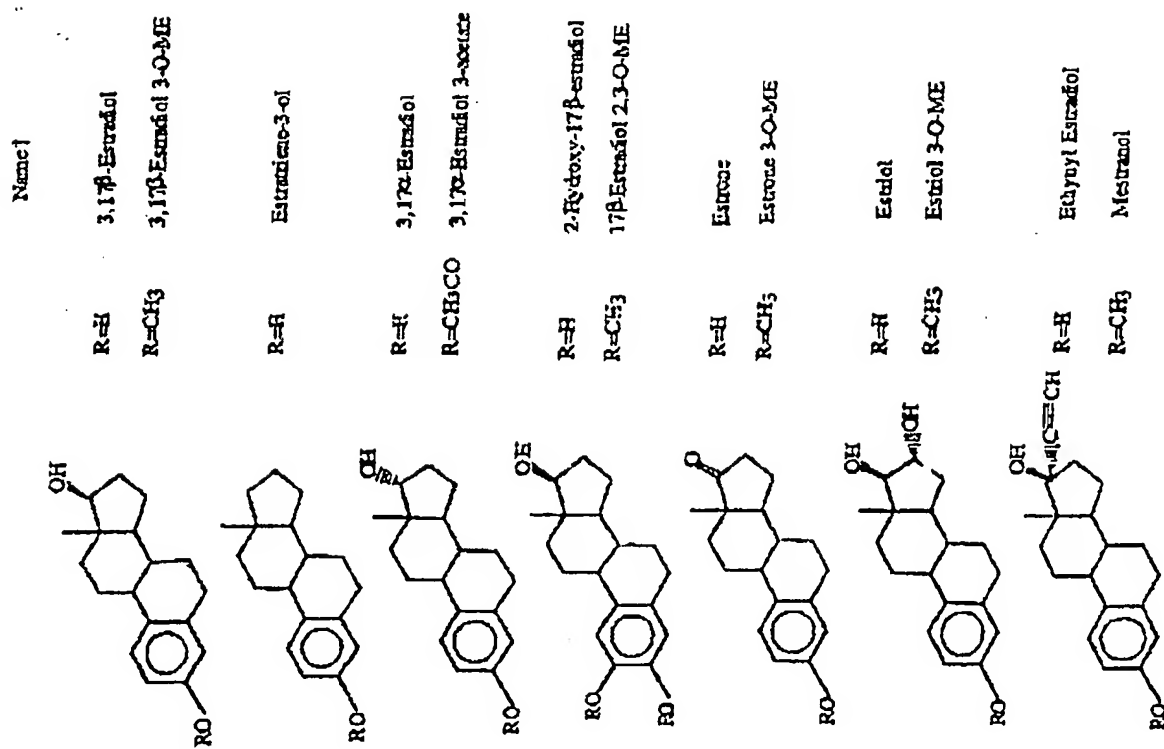


Figure 17

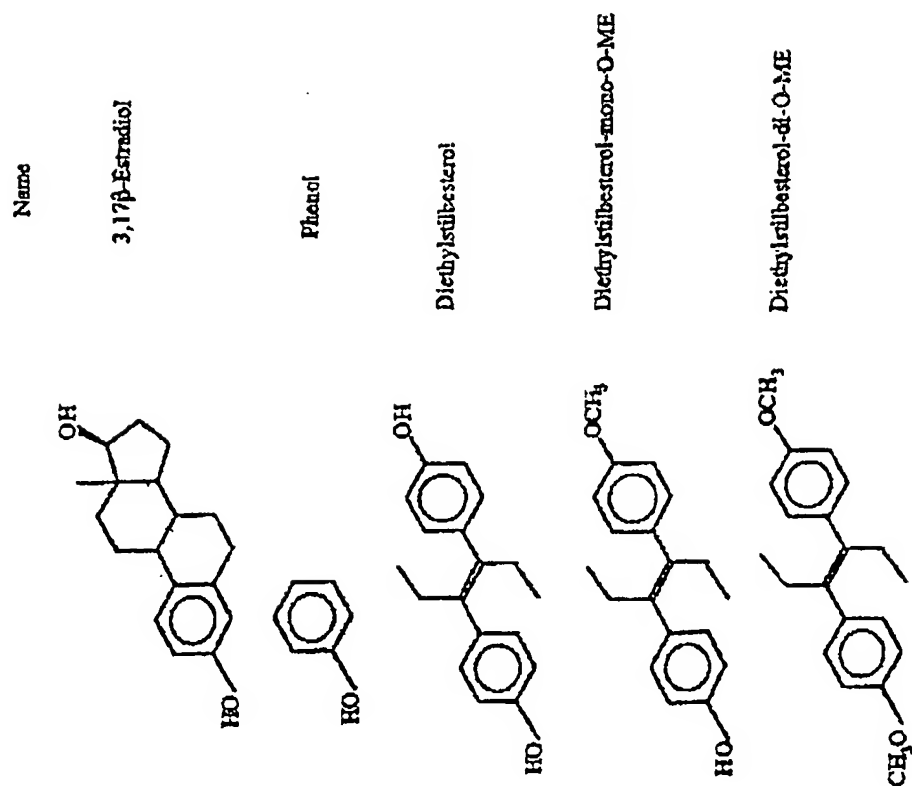


Figure 18

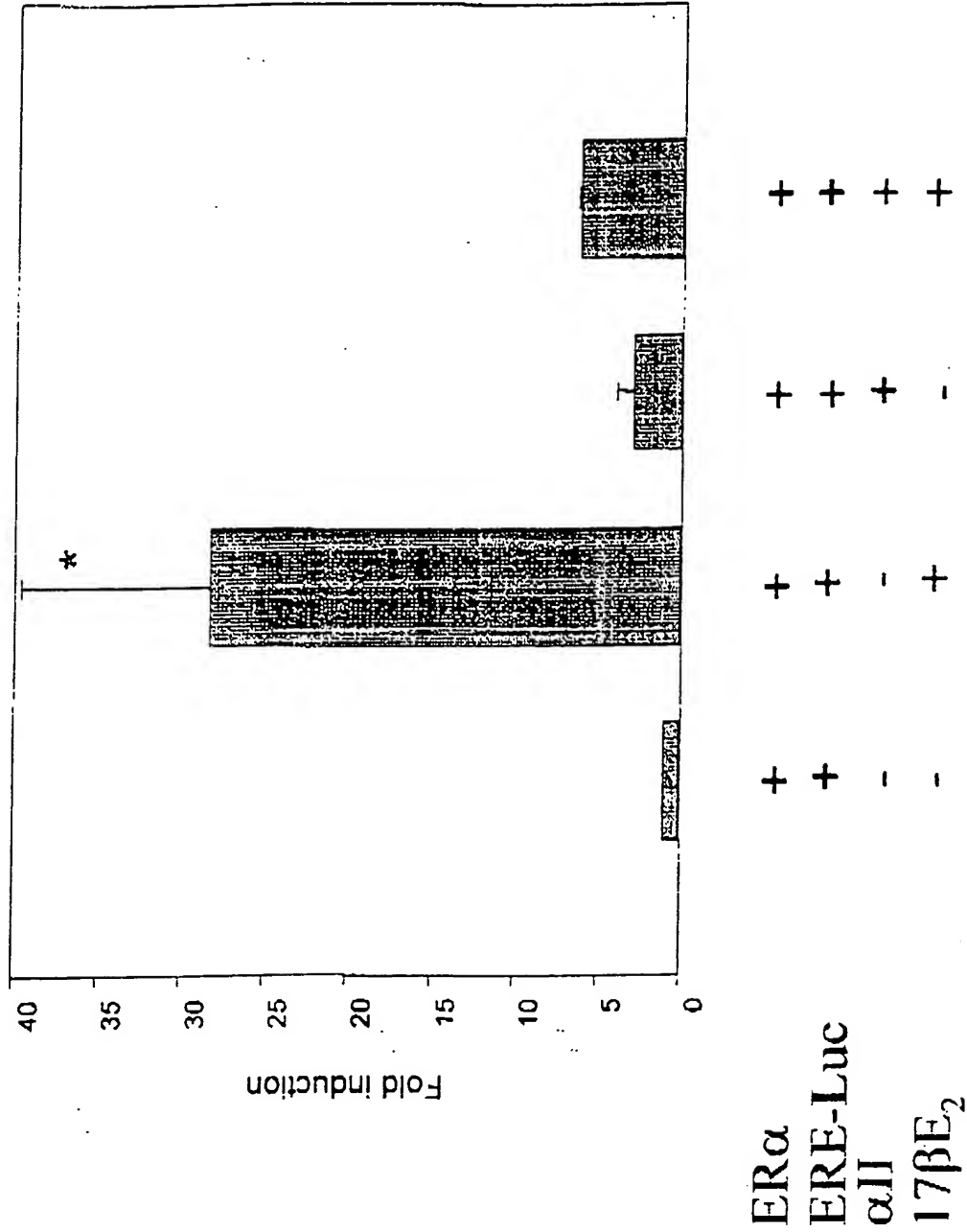


Figure 19: Effect of the all peptide on the 17βE₂-induced ERE activity in 293 cells

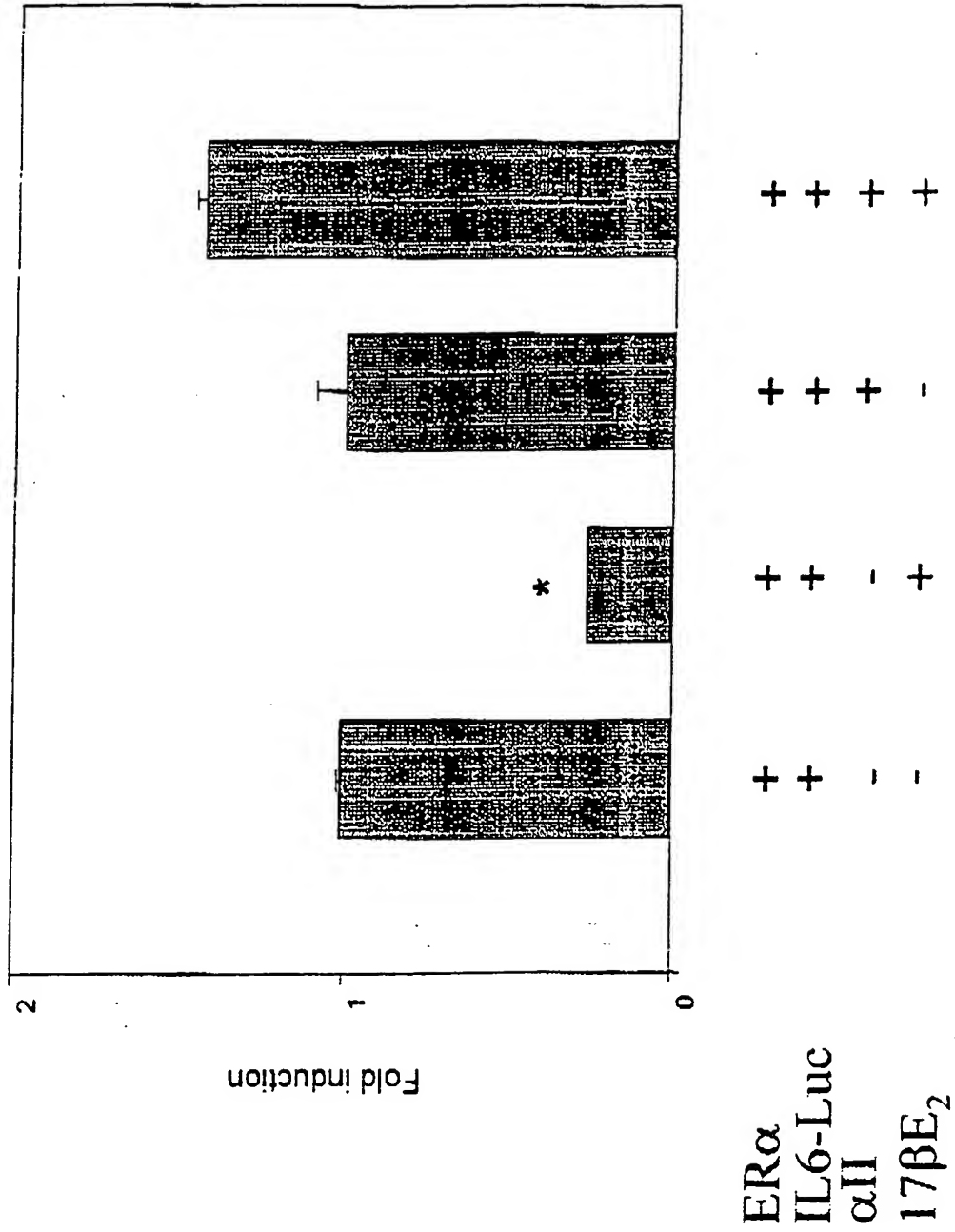


Figure 20: Effect of the all peptide on the 17βE₂-induced inhibition of IL-6 activity in 293 cells

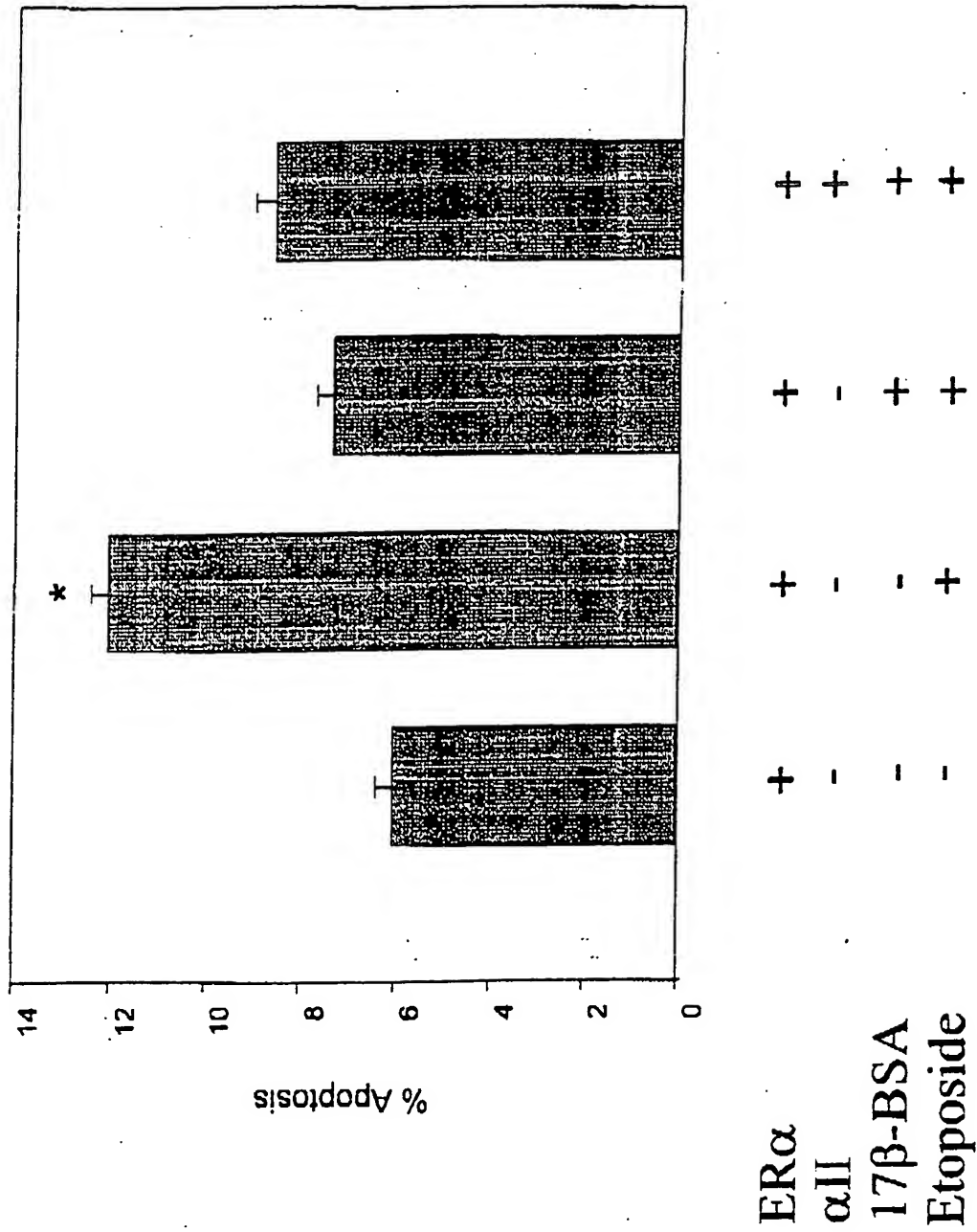


Figure 21: Effect of the all peptide on the Etoposide-induced apoptosis of 17b-BSA-activated 293 cells